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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/937,521	09/26/2001	Makoto Ito	1422-0493P	9464

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EXAMINER	
NASHED, NASHAAT T	
ART UNIT	**PAPER NUMBER**
1652	

DATE MAILED: 10/29/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/937,521	Ito, M.
Examiner	**Art Unit**
Nashaat T. Nashed	1652

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Sep 26, 2001*.

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above, claim(s) *15-20* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-14* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☒ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). *2 & 7*
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

The application has been amended as requested in the communication filed September 26, 2001. Accordingly, claims 4, 5, 9, 11, 12, 14, 15 and 20 have been amended.

Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

Group I: Claims 1-14 are drawn to a nucleic acid encoding ceramidase, vector, and host cell comprising said nucleic acid, a recombinant method to make ceramidase, classified in class 435, subclass 195.

Group II: Claims 15, 18, and 19 are drawn to a antibodies and a method of use, classified in class 530, subclass 387.1.

Group III: Claims 16 and 17 are drawn to a hybridization method to detect nucleic acid, classified in class 435, subclass 6.

Group IV: Claim 20 is drawn to a method of controlling the amount of ceramide in a cell or tissue, classified in class 514, subclass 44.

The inventions listed as Groups I-IV do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: The special technical features of the inventions of Group I is nucleic acid sequence of claim 1. Group I comprises claims drawn to the polypeptide encoded by said nucleic acid, and a vector and a host cell comprising said nucleic acid as well as a single method of using the nucleic acid. The special technical feature of the invention of Group II is the antibody which is different from the special technical feature of Groups I, III, and IV, i. e., the nucleic acid sequence. The special technical feature of Groups III and IV is the nucleic acid of Group I. The inventions of Groups III and IV represent a second and third use of the nucleic acid.

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined

process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.**

Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

During a telephone conversation with Marc Weiner on July 1, 2003 a provisional election was made with traverse to prosecute the invention of Group I, claims 1-14. Affirmation of this election must be made by applicant in replying to this Office action. Claims 15-20 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Acknowledgment is made of applicant's claim for priority based on an applications filed in Japan on March 26, 1999.

The disclosure is objected to because of the following informalities: The specification contains several undefined abbreviation or acronyms, see for example C12-NBD ceramide on page 9, and GM1a and NMD in Table 1 on page 10.

Appropriate correction is required.

The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

The claims are generally narrative and indefinite, failing to conform with current U.S. practice. They appear to be a literal translation into English from a foreign document and are replete with grammatical and idiomatic errors. In addition, it is recommended to delete the phrase "of the sequence listing" after every occurrence of a sequence identification number. Since the sequence listing is a required part of the disclosure, the phrase "of the sequence listing" after a sequence identification number is redundant and unnecessary.

Claims 2 and 10 are objected to because of the following informalities: The claims contain square brackets which may be mistaken for an amendment to delete the phrase in the square brackets. The examiner suggests that the phrase "a reaction mixture [composition:" should be substituted with -----a reaction mixture comprising---- and deleting the second bracket from the claim. Appropriate correction is required.

35 U.S.C. § 101 reads as follows:
"Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title".

Claims 1-3, and 8-14 are rejected under 35 U.S.C. § 101 because the claimed invention is directed toward non-statutory subject matter.

In the absence of the hand of man, naturally occurring proteins and/or nucleic acids are considered non-statutory subject matter. *Diamond v. Chakrabarty*, 206 USPQ 193 (1980). This rejection may be overcome by amending the claims to contain wording such as "An isolated and purified protein or nucleic acid".

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-14 are rejected under 35 U.S.C. § 112, first paragraph, as the disclosure is enabling only for claims limited to nucleic acid encoding the mouse ceramidase of SEQ ID NO: 14 including SEQ ID NO: 15 as well as nucleic acid sequences which hybridize to SEQ ID NO: 15 under the specific stringent hybridization and wash conditions described in the specification on page 43, lines 16-21. The specification does not enable any person skilled in the art to make and use the invention commensurate in scope with these claims. The claims are broader than the enablement provided by the disclosure with regard to all

possible ceramidase having any substrate specificity from any biological source that differ from the amino acid SEQ ID NO: 14 and nucleic acid sequence of SEQ ID NO: 15 by at least one or more deletion, insertion, substitution and combination thereof. Since all proteins are related to each other and made of 20 naturally occurring amino acids and the nucleic acid sequence are made of the four naturally occurring deoxyribonucleotide or nucleotides, the claims read on any nucleic acid encoding or ceramidase from any biological source and their mutants, part (C and D) of claim 1. The word "having" in claim 8 is taken to mean comprising and, thus, claim 8 is directed to any polypeptide comprising undefined number of contagious amino acid residues of SEQ ID NO: 14. Factors to be considered in determining whether undue experimentation is required, are summarized *In re* Wands [858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)]. The Wands factors are: (a) the quantity of experimentation necessary, (b) the amount of direction or guidance presented, (c) the presence or absence of working example, (d) the nature of the invention, (e) the state of the prior art, (f) the relative skill of those in the art, (g) the predictability or unpredictability of the art, and (h) the breadth of the claim.

The nature and breadth of the claimed invention encompasses any nucleic acid and polypeptide having any degree of sequence homology to SEQ ID NO's: 15 and 14, respectively, which having or encoding any ceramidase activity from any biological source. Also, the claims are drawn to any insertion, deletion, substitution and combination thereof mutants. The specification provides guidance and examples in the form of an assay to purify the ceramidase from mice livers (example 1), clone the gene of SEQ ID NO: 15 encoding the ceramidase of SEQ ID NO: 14, heterologous expression of the protein in mammalian host cell (examples 2-5), and cloning the same enzyme from the mice brain (example 6). Also, the specification teaches the substrate specificity for the enzyme in Table 1 on page 10. While molecular biological techniques and genetic manipulation to make and use the constructs claimed are known in the prior art and the skill of the artisan are well developed, knowledge regarding the biological source of all possible nucleic acid encoding natural/alkaline ceramidase which has any degree of sequence homology to SEQ ID NO's: 14 or any degree of sequence homology to SEQ ID NO: 15, the three dimension structure of the protein of SEQ ID NO: 14, the amino acids required for the catalytic activity and proper folding of the protein, and the location of amino acid residues in SEQ ID NO: 14 which can be deleted, substituted, inserted is lacking. Thus, searching for a ceramidase having any specificity which differs from that of SEQ ID NO: 14 by any number of deletion, substitution, insertion and combination thereof of one or more amino acid residues is well outside the realm of routine experimentation and predictability in the art of success is extremely low. The amount of experimentation requires to identify a protein homolog of SEQ ID NO: 14 and the nucleic acid encoding such a homolog is enormous. Since routine experimentation in the art does not include screening vast numbers of genomic, cDNA, and man-made DNA libraries where the expectation of obtaining the desired ceramidase with a desired activity is unpredictable, the Examiner

finds that one skilled in the art would require additional guidance, such as information regarding the biological source of the enzyme, the three dimension structure of the protein, and the nucleic acid and amino acid sequences for the desired ceramidase, and a method of redesigning the ceramidase of SEQ ID NO: 14 to any amino acid sequence having any ceramidase activity. Without such a guidance, the experimentation left to those skilled in the art is undue.

Claims 1-14 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following are the reasons for the rejections:

(a) The phrases "a polypeptide having the amino.....a partial sequence thereof" in claim 1(A) and (B) and 8, "deletion, addition, insertion or substitution of at least one amino acid residue/base" in claim 1(C) and (D), "at least one base" in claim 1(D), "stringent conditions" in claim 1(E), and in claim 1(F) render the claims indefinite because the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. For examination purposes only, the phrases are taken to mean the following: (a) "a polypeptide having the amino .....a partial sequence thereof": a protein comprising a fragment thereof; (b) "deletion, addition, insertion or substitution of at least one amino acid residue/base": any protein/polypeptide, or nucleic acid, (c) "at least one base": taken to mean "at least one nucleotide" which makes claimed the nucleic acid sequence any nucleic acid. It is noted that the application define the phrase stringent hybridization conditions on page 15, but it does not describe a wash conditions which determine the degree of stringency. On page 43, there is another hybridization and wash conditions described as stringent condition. The rejection of the phrase "stringent conditions" would be vacated if the phrase is defined in the claim by the definition on page 43 which include hybridization and wash conditions. The phrase "above (A) to (E) via degeneracy" is confusing the claim because sections (A) and (C) are directed to all nucleic acid encoding an amino acid sequence, i. e., all the variant nucleic acid sequences due to the degeneracy of the genetic code encoding an amino acid sequence.

(b) Claims 2, 3, and 10 contain abbreviations or acronyms such as C12-NBD-ceramide, GM1a and sulfatide which render the claims indefinite because the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. The specification does not define the abbreviation and one of ordinary skill in the art does not know what they are.

(c) The phrase "capable of specifically hybridizing to the gene" in claim 14 renders the claim indefinite because the resulting claim does not clearly set

forth the metes and bounds of the patent protection desired. Since most nucleic acid sequences are expected to hybridize "specifically" to any other nucleic acid sequence under a given set of conditions, the phrase is considered indefinite.

(d) claims 4-7, 9, and 11-13 are included in this rejection because they are dependent on a rejected claim and do not cure its deficiencies.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in-

(1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or

(2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

Claims 11 and 12 are rejected under 35 U.S.C. § 102(b) as being anticipated by the fact that all four DNA or RNA nucleotides are commercially available or known in the prior art. The phrase "part thereof" in claims 11 and 12 reads on a single nucleotide.

Claims 1, 2, 4-7, 9-11, and 14 are rejected under 35 U.S.C. § 102(e) as being anticipated by Akino *et al.* (U. S. Patent 6,258,581).

The patent teaches a polypeptide of SEQ ID NO: 1 having ceramidase activity from *Psedomonas aeruginosa* and encoded by the gene of SEQ ID NO: 2, see the abstract. Both the nucleic and amino acid sequences consists of natural amino acids and nucleotides. Thus, the nucleic and amino acid sequences taught by the patents must be related to the nucleic and amino acid sequences of SEQ ID NO's: 15 and 14 respectively, by deletion, insertion, substitution and combination thereof of at least one nucleotide or amino acid residues (claims 1 and 9). Also, the patent teaches primer and hybridization probes, see column 7 (claims 11 and 14), lines 1-20 and 49 through column 12, line 5, and

the construction of a vector and a host cell comprising the nucleic acid (claims 4-6), as well as a method of producing the polypeptide in an *E. coli* host cell (claim 7), see example 1-3). While the patent does not teach specifically that the ceramidase from *P. aeruginosa* catalyzes the hydrolysis of C12-NBD-ceramide, such a catalytic property is an intrinsic property of the taught ceramidase (claims 2 and 10). Evidence supporting that the enzyme taught in the patent catalyzes the specific substrate C12-NBD-ceramide is found in the prior art of record, see Tani *et al.* (IDS: J. Biochem. April 1999, Vol. 125, pages 746-749).

Claims 1, 4-7, 9, 11, and 14 are rejected under 35 U.S.C. § 102(b) as being anticipated by Koch *et al.* (IDS: J. Biol. Chem. 1996, Vol. 271, 33110-33115).

Koch *et al.* teach the cloning of a human ceramidase, see the abstract. They teach both the nucleic and amino acid sequences of the human enzyme in Figure 1 which shows that they consists of natural amino acids and nucleotides. Thus, the nucleic and amino acid sequences taught by Koch *et al.* must be related to the nucleic and amino acid sequences of SEQ ID NO's: 15 and 14 respectively, by deletion, insertion, substitution and combination thereof of at least one nucleotide or amino acid residues (claims 1 and 9). Also, the Koch *et al.* teach primers and hybridization probes(claims 11 and 14), see the paragraph bridging pages 33111 and 33112, and the construction of a vector and a host cell comprising the nucleic acid (claims 4-6), as well as a method of producing the polypeptide in a COS-1 host cell (claim 7), see the paragraph bridging the two columns on page 33112).

Claim 14 is rejected under 35 U.S.C. § 102(b) as being anticipated by Marra *et al.* (Database: EST, Accession number AA920146).

The EST teach a nucleic acid sequence consisting of 451 nucleotide in which residues 1-157 are identical to residues 1893-1049 of SEQ ID NO: 15 of the instant application. The EST would be expected to hybridize to the nucleic acid sequence of SEQ ID NO: 15 under some hybridization conditions.

Claims limited to the ceramidase of SEQ ID NO: 14 or encoded by nucleic acid sequence which hybridizes to SEQ ID NO: 15 under the high stringent conditions and wash conditions on page 43 and nucleic acid encoding the same would be considered favorably.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nashaat T. Nashed, Ph. D. whose telephone number is

(703) 305-6586. The examiner can normally be reached Monday, Tuesday, Thursday, and Friday from 9:00 a.m. to 5:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, can be reached on (703) 308-3804. The fax phone numbers for this Group are (703) 305-3014 and (703)308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Nashaat T. Nashed, Ph. D.
Primary Examiner